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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,874	08/20/2003	Kenneth F. Buechler	36671-744.502	8658

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
08/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,874	BUECHLER ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-33 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-33 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *July 20, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 23, 2009 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-33 and 43-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test to determine whether a claimed invention is enabled is whether a person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Whether there would be undue

experimentation to claimed invention is determined by analyzing the factors set out in the *Wands* case. Known as the Wands factors, they include (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples and (8) the quantity of experimentation needed to make or use the invention based on the content of the content of the disclosure. *In re Wands*, 8 USPQ2d at 1404. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

I. Wands Factors

The Wands factors are described in depth below.

i. Breath of the claims

The claims are broad, directed to inhibiting degradation of BNP (77-108) or BNP (1-108) by administering any prolyl-specific dipeptidyl peptidase ("DPP") inhibitor to a subject. *See e.g.*, claims 29, 32 and 43. The inhibitor is not limited to any particular type of compound, nor is the manner of administration specified.

ii. Nature of the invention

The invention is directed to a method of inhibiting degradation of BNP (77-108) or BNP (1-108) by administering a DPP inhibitor to a subject. The DPP inhibitor prevents any DPP from cleaving proline in the penultimate position of BNP (77-108) or BNP (1-

108), thereby preventing their degradation. *See* Specification, paragraph 0046. This inhibition allows BNP (77-108) to perform its natural function of regulation blood pressure and fluid balance. *Id*. at paragraph 0005. The inhibition also improves the potential for BNP to act as a therapeutic agent. *Id*. at paragraph 0046.

iii. State of the prior art

The prior art describes using various sections of the full-length BNP molecule as a marker for various diseases, including congestive heart failure. *See* Cheng *et al*., J. Am. Coll. Cardio. (2001) 37:386-391 ("Cheng") (using the mature portion (BNP (77-108))); U.S. Patent No. 5,786,163 to Hall (using BNP (1-76)) and U.S. Patent No. 6,124,430 to Mischak *et al* ("Mischak") (using portions between amino acids in the 1 and 25 position). The prior art also describes that a DPP inhibitor can be administered to a patient to treat congestive heart failure. *See* U.S. Patent App. Pub. No. 2004/0167341 to Haffner *et al.* ("Haffner"). Haffner, however, does not appear to provide sufficient guidance on using a DPP inhibitor for inhibiting the degradation of BNP molecules in a subject selected based on congestive heart failure or the other two claimed diseases. Indeed, Applicants make this argument in traversing the combination of Cheng and Haffner used to reject claims 29-33 and 43-49. *See* Response filed August 7, 2009. Instead, Haffner appears to generally teach inhibiting DPP to treat a variety of diseases with no specific guidance on how DPP operates. *See* '341, the entire document. Accordingly, the prior art describes various portions of BNP useful as markers for congestive heart failure, but does not teach administering a DPP inhibitor to inhibit degradation of the specific BNP peptides of BNP (77-108) and BNP (1-108).

iv. Level of one of ordinary skill

The level of ordinary skill is high.

v. Level of predictability in the art

The level of predictability in the art is extremely low. As noted above, the prior art provides ample description of using different portions of BNP as a marker for congestive heart failure, including BNP (77-108), but does not provide sufficient guidance for administering a DPP inhibitor to inhibit degradation of this BNP or BNP (1-108) in a subject with congestive heart failure, acute coronary syndrome or acute myocardial infarction. Indeed, Haffner, as the only reference that describes using a DPP inhibitor to treat congestive heart failure, merely cites the disease in a prophetic example under a long list of diseases that Haffner alleges can be treated with the inhibitor. Applicants strongly argue this point in their previous responses, highlighting the unpredictability of the prior art in establishing that a DPP inhibitor can prevent the degradation of any BNP peptide, much less BNP (77-108) and BNP (1-108).

vi. Amount of direction provided by the inventor

Applicants have provided little direction to allow one of ordinary skill in the art to successfully practice the claimed invention. Indeed, Applicants only provide a general description on how DPP inhibitors operate *in vivo* with no concrete direction or steps in how to effectuate such inhibition. For example, paragraphs 0127 and 0129 generally describe steps for selecting and screening for DPP inhibitors, but do not relate these steps for selecting specific DPP inhibitors that would work on inhibiting BNP degradation. Instead, Applicants refer to prior art describing specific DPP inhibitors for

managing diabetes. *See* paragraph 0126. However, diabetes does not appear to have any relationship to congestive heart failure, acute coronary syndrome or acute myocardial infarction with respect to DPP inhibition. The general preparatory methods are therefore too broad to provide the skilled artisan with insight on how to select DPP inhibitors specific for the claimed invention.

vii. Existence of working examples

Applicants have not provided any working examples germane to showing that a DPP inhibitor can actually prevent degradation of BNP (77-108) or BNP (1-108) *in vivo*. Indeed, the only relevant working examples provided describe the assaying of BNP without reference to obtaining sample from a subject (Example 3), synthesis of DPP inhibitors without describing their use *in vivo* (Example 4) and the purification and assay of DPP peptides. None of these examples actually describe a process of selecting an appropriate DPP inhibitor for inhibiting degradation of BNP (77-108) or BNP (1-108), administering the inhibitor to a subject, and then assaying a biological sample from the subject to determine whether BNP inhibition has taken place.

viii. Quantity of experimentation needed

The quantity of experiment needed is great. As noted above, the prior art does not provide guidance on which DPP inhibitors are appropriate to inhibit degradation of BNP molecules. Moreover, Applicants' specification lacks any guidance or working examples for doing the same or indicating that such inhibition actually occurs. Accordingly, one of ordinary skill in the art would not be able to perform the claimed invention without undue performing undue experimentation.

II. Analysis of the Wands Factors

With the foregoing analysis in mind, one of ordinary skill in the art would not be able to perform the claimed invention without undue experimentation. Indeed, the claims are broad - directed to a method of using any DPP inhibitor for inhibiting degradation of specific BNP molecules *in vivo*; however, neither the prior art nor Applicants' specification provides sufficient guidance for accomplishing this method. Applicants acknowledge that the prior art is lacking in sufficient description. However, Applicants themselves have not provided sufficient information in the form of working examples or other guidance to allow the skilled artisan to practice the invention without performing undue experimentation. Accordingly, the instant claims are rejected as lacking enablement.

Claims 29-33 and 43-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claims as amended recite BNP (1-108) in the context of both specifically detecting the peptide and administering an inhibitor of DPP to inhibit degradation of the peptide. The specification, however, does not provide support for specifically detecting BNP (1-108) in an assay. Indeed, the specification does not even mention this peptide when discussing different peptides of BNP that can be detected.

See paragraphs 0005, 0016-0017, 0026-0027, 0036-0037, 0041-0042 and 0056-0057. Although paragraph 0058 describes the sequence of BNP (1-108), it does not describe the sequence in the context of performing an assay to detect the sequence. Accordingly, there is no specific description of BNP (1-108) being detected in an assay. Lacking such a description, the specification does not provide written description support for performing an assay to specifically detect BNP (1-108).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-33 and 43-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 29, 32 and 43 each recite four steps: a selecting step, a performing step, a determining step and administering step. It is clear that the performing step follows the selecting step and the determining step follows the performing step. However, it is unclear how the administering step relates to the foregoing three steps. It is presented with no link to the other steps. Accordingly, the administering step renders the claims vague and indefinite.

For prior art purposes, the administering step is interpreted as resulting from the treatment regimen.

Dependent claims 30-31, 33 and 44-49 are vague and indefinite for the same reason.

Response to Arguments

Applicant's arguments in the response filed December 23, 2009, with respect to the rejection of claims 239-33 and 43-49 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejection under 35 U.S.C. 112, first paragraph are presented above.

Note that claim 50 is rejected only for lacking written description of BNP (1-108).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Unsu Jung/
Primary Examiner, Art Unit 1641